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10/713,898	10/18/2002	David C. Schwartz	960296.99047	4216

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EXAMINER	
MUMMERT, STEPHANIE KANE	
ART UNIT	**PAPER NUMBER**
1637	

NOTIFICATION DATE	DELIVERY MODE
04/25/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/713,898	SCHWARTZ ET AL.	
	Examiner	Art Unit	
	STEPHANIE K. MUMMERT	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 December 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *21 and 23-27* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21 and 23-27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendment filed on December 27, 2007 is acknowledged and has been entered. Claim 22 has been canceled. Claims 21 and 23-27 are pending.

Claims 21 and 23-27 are discussed in this Office action.

All of the amendments and arguments have been thoroughly reviewed and considered but are not found persuasive for the reasons discussed below. Any rejection not reiterated in this action has been withdrawn as being obviated by the amendment of the claims. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

This action is made NON-FINAL due to reformulation of rejections and clarification of the explanation of priority afforded to specific claims.

Previous Rejections

Claim Interpretation

The term 'microchannel' is being given the broadest reasonable interpretation in light of the specification. The term is not explicitly defined in the specification and the term is instead described in general terms and includes preferred embodiments. For example, the specification notes "the present invention fixes and straightens polymeric molecules using a channel sized to provide laminar flow of a liquid along a channel length, the channel having at least a first wall providing electrostatic attraction to the polymeric molecule" (paragraph 13 of PgPub). The

specification also teaches "the channel may include a region of varying cross-section to promote a gradient in the laminar flow rate" (paragraph 29 of PgPub). Finally, regarding more specific dimensions, the specification notes "in one embodiment, the cross-sectional width of the micro-channel is 50 micrometers and is preferably less than 100 micrometers. More generally, it is believed that the width will be between one and one hundred times the straightened length 40 of the polymeric molecule" (paragraph 51 of PgPub). While this portion of the specification suggests specific size of the microchannel, this teaching does not reach to the level of a specific definition of the size at which a channel of the invention is a microchannel. Therefore, as the term has no specific size limitations associated with it, the term is being given the broadest reasonable interpretation and is being interpreted as reading on application of the method to a 'channel' of any size.

Regarding the term 'wall', the term is not given a specific definition and therefore is being given the broadest reasonable interpretation in light of the specification and is being interpreted as reading on DNA affixed or attached to any surface, including a rounded particle or bead.

New Grounds of Rejection

The statement of lack of support in the priority documents has been adjusted in response to the request from Applicant and to correct a typographical error for application no. 09/962802, which corresponds to US Patent 6,610,256.

The art rejections have also been reformulated to remove the Miyachi reference and to clarify the grounds for obviousness. The rejection of claim 23 has been corrected and is properly rejected under 35 USC 103 in view of Kambara and Bensimon and not only under Kambara.

Priority

The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application). The disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

The disclosure of the prior-filed application, Application No. 09/962802 (US Patent 6610256), 08/855410 (US Patent 6294136) and 08/415710 (US Patent 5720928), fails to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application. Each of these patent disclosures and claims are directed to practice of the method on a planar surface and do not disclose of otherwise provide support for the practice of the method in channel or microchannel formats as claimed in the instant specification. The only mention of channels or microchannels present in these prior filed applications is the use of a microchannel plate reader, a disclosure which does not support the method of straightening or fixing within a channel.

Claim Rejections - 35 USC § 103

1. Claims 21, 23-25 and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kambara et al. (US Patent 5,356,776; October 1994) in view of Bensimon et al. (US Patent 6,265,153; July 2001). Kambara teaches a method of fixing and straightening DNA molecules in a channel (Abstract).

With regard to claim 21, Kambara teaches a method of straightening and fixing polymeric molecules comprising the steps of:

(a) putting the polymeric molecules in a carrier liquid (col. 3, lines 48-57, where the terminus of the DNA is fixed and stretched via fluid flow; col. 4, lines 1-17),

(b) passing the polymeric molecules and carrier liquid through a micro-channel to promote a laminar flow of carrier liquid in the micro-channel causing the polymeric molecule to achieve a straightened configuration (Figure 8, col. 4, lines 1-17, where the terminus is labeled and the opposite terminus is bound or affixed to a particle, and the DNA affixed to the wall/particle is passed in a carrier liquid through a microchannel; see Example 4, col. 10, lines 48-65, where the dimensions of the channel are provided; liquid flow is used to fix the particle and stretch the DNA and therefore meets the limitation of a laminar flow and the polymer is straightened).

With regard to claim 24, Kambara teaches an embodiment of claim 21 further including the step of (d) optically inspecting the straightened polymeric molecule attached to the first wall (Example 4, col. 10, where following stretching in the microchannel, the DNA is optically inspected to determine the position of the label at the opposite end of the molecule, see especially lines 65-67).

With regard to claim 25, Kambara teaches an embodiment of claim 21 further wherein step (b) first causes a straightening of the polymeric molecule in the laminar flow and second causes attachment of one end of the polymeric molecule to the first wall and third causes attachment of the length of the polymeric molecule to the wall (Figure 8, col. 4, lines 1-17, where the terminus is labeled and the opposite terminus is bound or affixed to a particle, which meets the limitation of a wall attractive to the polymeric molecule, and the DNA affixed to the wall/particle is passed in a carrier liquid through a microchannel; see Example 4, col. 10, lines 48-65, where the dimensions of the channel are provided; liquid flow is used to fix the particle and stretch the DNA).

Regarding claims 21, 24 and 25, while Kambara does not teach direct attachment to the first wall of the channel, Kambara instead teaches attachment to a different wall, specifically the bead, which meets the limitation of a wall of the channel. However, the bead with the molecule attached is fixed relative to the first wall and therefore 'attaches' the polymer to the first wall. Bensimon teaches a process for aligning a macromolecule onto the surface of a support and attaching the molecule to the first wall (Abstract).

With regard to claim 21, Bensimon teaches having a first wall (col. 3, lines 11-17, where the support of Bensimon can take many forms, including beads or particles) electrostatically attractive to the polymeric molecule (col. 3, lines 58-65, where the adsorption of the macromolecule onto the surface can be controlled through surface charges and the electrostatic interactions between the surface and the molecule; col. 4, lines 52-61, where specific types of surface functionalities are described; see also col. 5, lines 4-23, for example) and causing the polymeric molecule to adhere in straightened configuration to the first wall (Example 1, col. 17,

lines 39-46, where capillary force on the DNA molecule(s) is sufficient to stretch the molecule; col. 4, lines 4-6, where it is noted that one aligned, the molecules adhere strongly to the surface).

With regard to claim 27, Bensimon teaches an embodiment of claim 21 further including the step of treating at least one wall of the microchannel to have a positive surface charge of predetermined density (col. 3, lines 58-65, where the adsorption of the macromolecule onto the surface can be controlled through surface charges and the electrostatic interactions between the surface and the molecule; col. 4, lines 52-61, where specific types of surface functionalities are described; see also col. 5, lines 4-23, for example).

With regard to claim 23, Bensimon teaches an embodiment of claim 21 further including the step of (d) applying restricting enzymes to the straightened polymeric molecule attached to the first wall (col. 12, lines 53-58, where physical mapping of genomic DNA can be carried out through a method comprising the steps of extraction, purification, cleavage with restriction enzyme followed by 'combing' on surfaces).

Regarding claim 23, Bensimon teaches that the method of physical mapping of polymeric molecules comprises thorough restriction digestion followed by fixation and elongation. However, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to modify the order of method steps taught by Bensimon to arrive at the claimed invention with a reasonable expectation of success. As noted in the MPEP § 2144.04 IV C, "Ex parte Rubin , 128 USPQ 440 (Bd. App. 1959) (Prior art reference disclosing a process of making a laminated sheet wherein a base sheet is first coated with a metallic film and thereafter impregnated with a thermosetting material was held to render prima facie obvious claims directed to a process of making a laminated sheet by reversing the order of the prior art process

steps.). See also In re Burhans, 154 F.2d 690, 69 USPQ 330 (CCPA 1946) (selection of any order of performing process steps is prima facie obvious in the absence of new or unexpected results); In re Gibson, 39 F.2d 975, 5 USPQ 230 (CCPA 1930) (Selection of any order of mixing ingredients is prima facie obvious.)." Therefore, in the absence of new or unexpected results, it would have been prima facie obvious to one of ordinary skill in the art to adjust the order of the method steps taught by Bensimon to arrive at the claimed invention with a reasonable expectation for success.

Further regarding claim 21, neither Kambara or Bensimon explicitly teach the term of "detaching" the first wall from the microchannel. Bensimon teaches analysis of the straightened polymeric molecules stretched out on a slide or other planar surface (Example 3, col. 19, lines 21-26, where the adhered molecules are analyzed after removal of the coverslip; see also Figures 7-9). Therefore, it would have been prima facie obvious to remove the slide or planar support with the straightened molecules attached for further processing, achieving the limitation of the claim as recited.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have applied the teachings of Bensimon to the method of DNA stretching and analysis taught by Kambara to arrive at the claimed invention with a reasonable expectation for success. Kambara teaches a method comprising affixing one end of a DNA molecule to a bead, which comprises a broad interpretation of a wall of a channel, places the DNA in a channel that captures the polymer to a wall of the channel and stretches the DNA using fluid flow, or laminar flow. Bensimon teaches a very similar method of DNA analysis, however in this case an end of the DNA is fixed and the DNA is aligned along the length of a wall, which may comprise

a bead (col. 3, lines 11-17, where the support of Bensimon can take many forms, including beads or particles), through progress of a meniscus instead of by laminar flow.

In view of the common teachings between Bensimon and Kambara, it would have been prima facie obvious to one of ordinary skill in the art to incorporate the format of a surface electrostatically attractive to a polymeric molecule to promote both adherence and straightening of polymeric molecules as taught by Bensimon into the format taught by Kambara. Furthermore, while it is noted that neither Bensimon or Kambara explicitly teach the term detachment of a wall or bead from within a channel, it was well known to one of ordinary skill in the art at the time the invention was made how to remove a bead or other type of surface, particularly with DNA attached, from a support, for further processing or analysis. Bensimon specifically teaches "the combed YACs are denatured between two cover slips" and "the detection of hybrids is performed according to procedures known for in situ hybridizations" and "hybridized segments such as that shown in Fig. 10 are then observed by fluorescence microscopy" (Example 3, col. 19, lines 38-50). Therefore, despite the lack of specific teaching of the word detachment or detaching, it would have been prima facie obvious based upon the teaching of Bensimon of the desirability of having the stretched polymers or oligonucleotides present in a format available for further processing, analysis and detection, and therefore separate from the channel or means for separation. It also would have been prima facie obvious to envision a channel for straightening molecules using techniques including Bensimon and Kambara, and to include a format wherein the stretched DNA could be removed for further analysis while stretched on the surface. Therefore, as each of these elements were known in the prior art at the time of the invention and the combination of these elements would provide a predictable result, it would have been prima

facie obvious to one of ordinary skill in the art at the time the invention was made to have incorporated these elements to analyze straightened DNA molecules and then to recover these molecules following analysis through the removal of the bead or wall element from the other portions of the channel or support.

2. Claim 26 is rejected under 35 U.S.C. 103(a) as being unpatentable over Kambara in view of Bensimon as applied to claims 21, 23-25 and 27 above, and further in view of Kaiser et al. (Journal of Molecular Biology, 1963, vol. 6, p. 141-7). Kambara teaches a method of fixing and straightening DNA molecules in a channel (Abstract).

With regard to claim 26, Kaiser teaches an embodiment of claim 21 wherein the polymeric molecules are treated with a condensation agent to collapse the polymeric molecules into shear resistant balls and wherein step (a) includes the step of placing the polymeric molecules and carrier liquid into a reservoir attached to the micro-channel and decondensing the polymeric molecules in the reservoir prior to step (b) (Table 1, where specific concentrations of spermine are disclosed and p. 142, 'materials and methods' heading where DNA was isolated from bacteriophage λ and incorporated into the assay; p. 146, where it is noted that the protective effect may result from the formation of soluble aggregates).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have included the teachings of Kaiser, regarding the protection of nucleic acids through the inclusion of spermine to the method of DNA stretching and analysis taught by Kambara and Bensimon to arrive at the claimed invention with a reasonable expectation for success. As taught by Kaiser, "Spermine markedly protects DNA from breakage by rapid

stirring" (Abstract, line 1). Kaiser also teaches that "When λ DNA was stirred in the presence of spermine as shown in Table 1 neither the infectivity nor the ratio of turbid plaques to total plaques changed from their initial values." (p. 144, top paragraph). Finally, Kaiser concludes that "the data presented above show that polyamines, spermine in particular, protect λ DNA from breakage by rapid stirring" (p. 146, 'discussion' heading). The method taught by Kambara "a further important object of the present invention is to provide a process and apparatus for quickly measuring the length of not less than 1 megabase long DNA with high measurement precision" (col. 2, lines 42-45). Considering these teachings, Kambara expresses motivation to maintain the polymer sequence, either DNA or RNA, in an intact linear format in order to facilitate the distance measurements noted previously. Therefore, Kambara would have been motivated to incorporate solvents or steps directed specifically to the protection of the nucleic acid from breakage prior or during stretching. Therefore, considering the teachings of Kaiser towards the protective effects of spermine on DNA, one of ordinary skill in the art at the time the invention was made would have been motivated to incorporate spermine as taught by Kaiser into the method of DNA stretching and analysis taught by Kambara and Bensimon to achieve intact molecules prior to and during stretching and analysis.

Response to Arguments

Applicant's arguments filed December 27, 2007 have been fully considered but they are not persuasive.

Applicant's arguments with respect to claims 21 and 23-27 have been considered but are moot in view of the new ground(s) of rejection. However, insofar as the arguments apply over the current grounds of rejection, the arguments will be considered.

Applicant's arguments regarding the priority portion and the claim interpretation have been considered, but are not persuasive. Regarding priority, Applicant argues "the priority documents do refer to planar surfaces for optimal elongation and fixation... the general description of a laminar flow elongation device in the application is not so limited."

With apologies for the confusion, the statement regarding the lack of support has been amended for clarification. Specifically, the prior applications do not teach the straightening of polymers in a channel format, in any apparent manner. Therefore, these prior filed applications do not have support for the method as claimed.

Applicant's arguments regarding the claim interpretation are noted. However, it is noted that despite the well-known terminology of microchannel or channel, the specification is not clear regarding this term and the method is broadly claimed and therefore this term is also being given a broad interpretation in light of the specification. This same argument applies for the term "wall." The plain meaning of the term wall may imply a planar surface. However, Applicant argues in the response (p. 8) that while the optimal elongation may occur on a planar surface, the "elongation device in the application is not so limited and does not specify any requirement for a planar surface". Therefore, if the application is not limited to a planar surface

with the inclusion of the term "wall", the term can be applied to virtually any surface, including those that are not strictly planar, such as beads. The claim interpretation stands.

Applicant's arguments with respect to claim 23 have been considered but are not persuasive. Applicant asserts "changing the order of steps here would completely defeat the purpose of Applicant's invention which employs intact, elongated molecules fixed in the channel before cleaving such that the natural order of fragments can be visualized" (p. 11 of remarks).

These arguments are noted. It is agreed that if the order of steps were as applied in Bensimon alone, the limitation would not be met and would "yield a jumbled collection of molecules" as argued by Applicant. However, Applicant is misinterpreting the grounds of rejection. The rejection is based on the argument that it would have been obvious to take the teaching of Bensimon of cleavage followed by straightening and to change the order of steps. In this changed order based on the teaching of Bensimon in view of Kambara, the polymer would be straightened using the method of claim 21 and the straightened polymer would then be exposed to restriction enzymes. Considering the teachings of Bensimon and Kambara regarding further analysis of the straightened polymers, and considering that Bensimon teaches that restriction digestion is a useful method for physical mapping, it would have been obvious to change the order to achieve the method as claimed, not as taught by Bensimon. The rejection is maintained.

Applicant's arguments regarding claim 21, 24, 25 and 27 have been considered, but as the arguments apply to the rejection as previously stated and the rejection has been significantly

reformulated to better explain the position of obviousness based on the teachings of Kambara and Bensimon alone, the arguments are moot and it is difficult to respond to them more fully. In short, the rejection has been reformulated to clarify the wall, which wall is attractive to the polymer, and how each and every limitation of the claims are considered obvious over the art of record.

The reason in support of the obviousness rejection has also been changed in an effort to clarify the obviousness rejection.

Relevant Prior Art

3. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Chan et al. (US Patent 6,696,022; February 2004) teaches stretching of long DNA molecules using flow in channels (Abstract).

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to STEPHANIE K. MUMMERT whose telephone number is (571)272-8503. The examiner can normally be reached on M-F, 9:00-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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